G18 SCN5A Gene Mutation Associated With Acute Myocardial Infarction

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The goal of this presentation is to describe the first sodium channel mutation to be associated with the development of an arrhythmic storm during acute ischemia.

This presentation will impact the forensic science community by presenting findings which suggest that a loss of function mutation in SCN5A gene (cardiac sodium channel) may predispose to ischemia-induced arrhythmic storm and sudden cardiac death.

Ventricular tachycardia and fibrillation (VT/VF) complicating Brugada syndrome, a genetic disorder linked to SCN5A mutations, and VF compli- cating acute myocardial infarction (AMI) have both been linked to phase 2 reentry. Because of these mechanistic similarities in arrhythmogenesis, the contribution of SCN5A mutations to VT/VF complicating AMI were examined.

Nineteen consecutive patients developing VF during AMI were enrolled. Wild-type (WT) and mutant SCN5A genes were co-expressed with SCN1B in TSA201 cells and studied using whole-cell patch-clamp tech- niques.

One missense mutation (G400A) in SCN5A was detected in a conserved region among the cohort of 19 patients. A H558R polymorphism was detected on the same allele. Unlike the other 18 patients who each developed 1-2 VF episodes during acute MI, the mutation carrier developed six episodes of VT/VF within the first 12 hours. All VT/VF episodes were associated with ST segment changes and were initiated by short-coupled extrasystoles. A flecainide and adenosine challenge performed to unmask Brugada and long QT syndromes were both negative. Peak G400A and G400A+H558R current were 70.7% and 88.4% less than WT current at - 35mV ($P \leq 0.001$). G400A current decay was accelerated and steady-state inactivation was shifted -6.39 mV ($V1/2$=-98.9±0.1 mV vs. -92.5±0.1 mV, $P \leq 0.001$). No mutations were detected in KCNH2, KCNQ1, KCNE1, or KCNE2 in the G400A patient.

The first sodium channel mutation to be associated with the develop- ment of an arrhythmic storm during acute ischemia is described. These findings suggest that a loss of function in SCN5A may predispose to ischemia-induced arrhythmic storm and sudden cardiac death.

Sudden Cardiac Death, Myocardial Infarction, Ventricular Fibrillation

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